of **24** was obtained: mp 227–229 °C dec; ^{1}H NMR (CD_3OD) δ 2.20 (m, 1 H), 2.54 (m, 1 H), 3.68 (dd, J = 12.1 and 5.8 Hz, 1 H), 3.76 (dd, J = 12.1 and 3.2 Hz, 1 H), 4.30 (m, 1 H), 5.35 (dm, J = 54.2, 1 H), 6.07 (dd, J = 16.4 and 3.4 Hz, 1 H), 6.09 (d, J = 8.0 Hz, 1 H), 8.21 (dd, J = 8.0 and 1.2 Hz, 1 H); IR (KBr) 3395, 1673 cm^{-1}; MS m/e 229 (M^+ – HCl); $[\alpha]_{589nm}$ +141.21° (c 0.99, 0.1 N HCl). Anal. Calcd for $C_9H_{12}N_3O_3F$–HCl: C, 40.69; H, 4.93; F, 7.15. Found: C, 39.22; H, 4.85; F, 6.55.

This material was used in the next step without further purification.

1-(2,3-Dideoxy-2-fluoro-β-D-*threo*-pentofuranosyl)cytosine (F-ddC). An aqueous solution of **24** (19.8 g, 74.5 mmol) in 320 mL of water was passed through an ion-exchange column (200 mL of Bio-Rex 9, OH^- form, 20–50 mesh; Bio-Rad) using 600 mL of 66% aqueous methanol as eluent. The combined fractions containing F-ddC were concentrated, and the residue was recrystallized from ethanol to give 15.0 g (87.8% yield) of F-ddC: mp 205–208 °C (lit.[1b] mp 205–208 °C); ^{1}H NMR (CD_3OD) δ 2.14 (dddd, J = 28.2, 14.9, 5.3, and 1.9 Hz, 1 H), 2.52 (dddd, J = 34.4, 14.9, 8.5, and 5.7 Hz, 1 H), 3.68 (dd, J = 12.0 and 6.0 Hz, 1 H), 3.72 (dd, J = 12.0 and 3.9 Hz, 1 H), 4.24 (m, 1 H), 5.28 (dm, J = 54.3 Hz, 1 H), 5.88 (d, J = 7.5 Hz, 1 H), 6.01 (dd, J = 8.2 and 3.2 Hz, 1 H), 7.87 (dd, J = 7.5 and 1.5 Hz, 1 H); IR (KBr) 3465–3200, 1640 cm^{-1}; MS m/e 229 (M^+); $[\alpha]_{365nm}$ +710.15° (c 1.027, H_2O). Anal. Calcd for $C_9H_{12}N_3O_3F$: C, 47.16; H, 5.28; N, 18.33; F, 8.29. Found: C, 46.92; H, 5.25; N, 18.05; F, 8.21.

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Benzotriazole as a Synthetic Auxiliary: Advantageous Syntheses of Substituted Diarylmethanes and Heterocyclic Analogues

Alan R. Katritzky,* Xiangfu Lan, and Jamshed N. Lam

Department of Chemistry, University of Florida, Gainesville, Florida 32611-2046

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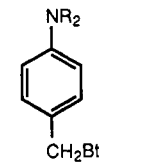
4-(Benzotriazol-1-ylmethyl)-*N*,*N*-dimethylaniline (**1b**) can be substituted at the CH_2 link via lithiation. Both the parent and substituted derivatives react with a variety of electron-rich benzenoid and heteroaromatic compounds in a novel approach to leuco dyes. Other 4-(benzotriazol-1-ylmethyl)anilines react similarly.

Introduction

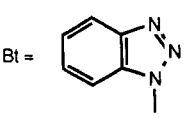
Di- and triarylmethanes containing electron-donating groups in ortho or para positions are of considerable importance. Thus they are leuco dyes which on hydride abstraction by oxidizing agents give colored cations of the type of Michler's hydrol, Crystal Violet, and Malachite Green. Previous synthesis of such di- and triarylmethanes generally involved the treatment of a one-carbon electrophilic reagent (formaldehyde, chloroform, etc.) with arene nucleophiles (usually substituted by electron donors such as NR_2, NHR, NH_2, OH) via an S_E2 mechanism.[1] Numerous reported vinylogous di- and triarylmethane dyes include a few heteroaromatic analogues.[2] For example, Naef[2b] synthesized trihetaryl dyes in yields of 20–85% by treatment of unsymmetrical dihetaryl ketones with 1,2-dimethylindole in the presence of phosphorus oxychloride. Other hetaryl dyes that have been prepared are diindolylpyridylmethanes,[2c] which afford colored compounds upon proton abstraction and hence cannot be considered as leuco dyes.

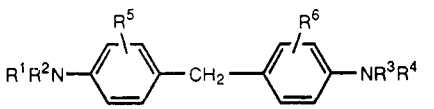
Compounds of type **2** have found numerous other applications in industry. They are used as curing agents for epoxy resins and urethane elastomers, as intermediates in the preparation of polyurethanes, in the synthesis of polyamides and in the production of dyes and recording materials.[3] Alteration of the molecule, such as by changing an aryl ring to a heterocyclic ring, or by introducing a functional group onto the methylene carbon, should modify the properties of these materials and perhaps widen their synthetic applications. Proper selection of these groups could lead to potential leuco dyestuffs.

Previous work[4] in our laboratory has shown that aniline or *N*,*N*-dialkylanilines are readily alkylated by 1-(hydroxymethyl)benzotriazole to give 4-(benzotriazol-1-ylmethyl)anilines **1**. Subsequent displacement of the benzotriazole group by arylamines or *N*,*N*-dialkylanilines gives either symmetrical or unsymmetrical 4,4′-methylenebis(*N*,*N*-dialkylanilines) **2**. Thus the displacement of benzotriazole by a variety of nucleophiles was investigated.



1a R = H
1b R = Me
1c R = Et





2

R^1-R^4 = H, alkyl
R^5, R^6 = H, alkyl, halogen

N-Benzylbenzotriazole has been shown to undergo lithiation at the benzylic carbon atom.[5] Although *N*,*N*-dimethylaniline and 4,4′-methylenebis(*N*,*N*-dimethylaniline) both undergo ortho-metalation (due to chelation effects),[6] it was anticipated that the electron-withdrawing nature of benzotriazole could assist in directing lithiation toward the benzylic position in **1**. We now report our results on the reaction of 4-(benzotriazol-1-ylmethyl)-

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(3) For more details, see ref 4 and references within.
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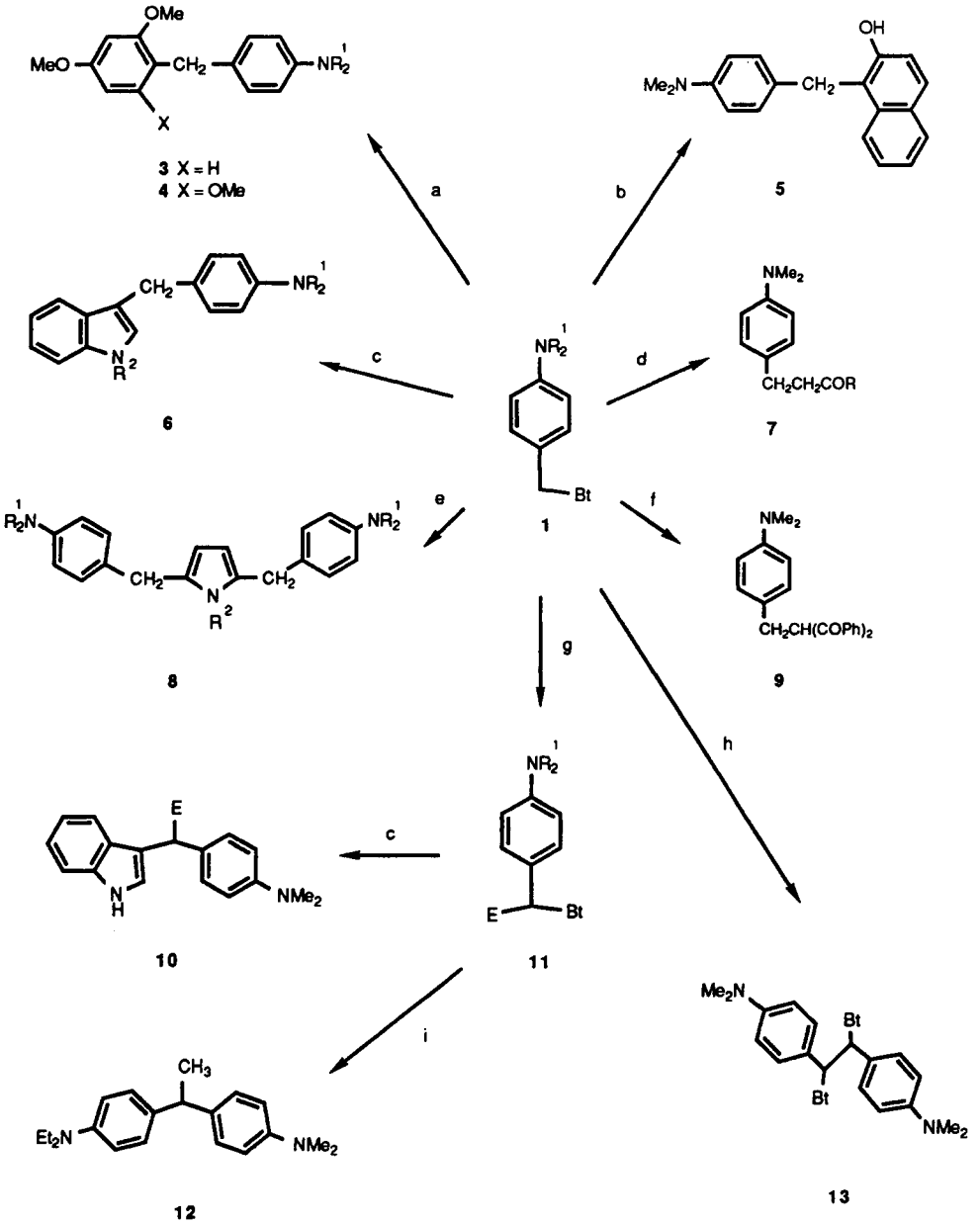
(5) Katritzky, A. R.; Lam, J. N. *Heteroatom Chem.* **1990**, *1*, 21.
(6) (a) Lepley, A. R.; Khan, W. A.; Giumanini, A. B.; Giumanini, A. G. *J. Org. Chem.* **1966**, *31*, 2047. (b) Friedmann, G.; Linder, P.; Brini, M.; Cheminat, A. *J. Org. Chem.* **1979**, *44*, 237.

0022-3263/91/1956-4397$02.50/0

Scheme I[a]



[a] (a) 1,3-Di- or 1,3,5-trimethoxybenzene; (b) 2-naphthol; (c) indole or *N*-methylindole; (d) $(RCO)_2CH_2$; (e) pyrrole or *N*-methylpyrrole; (f) (i) $(PhCO)_2CH_2$, $ZnBr_2$ (anhydrous), toluene, reflux; (ii) NaOH(aq); (g) (i) *n*-BuLi, THF; (ii) E^+, −78 °C to rt; (iii) H_2O; (h) (i) *n*-BuLi, THF, −78 °C; (ii) I_2; (i) *N,N*-diethylaniline; reaction conditions for **3–8**, **10**, **12**: (i) nucleophile, MeOH/H_2O, HCl, 75 °C; (ii) KOH(aq).

anilines **1** with various nucleophiles and on the introduction of functional groups at the methylene carbon via lithiation. Such synthetic elaboration followed by displacement of the benzotriazole residue as above is shown to offer a versatile new approach to diaryl- and diheteroarylmethanes.

Results and Discussion

The benzotriazole group in compounds of type **1** is now shown to be displaced efficiently by a series of electron-rich aromatic systems, including 1,3-dimethoxybenzene, 1,3,5-trimethoxybenzene, indoles, pyrroles, and 2-naphthol under reaction conditions similar to those for the synthesis of bisanilines (Scheme I, Table I).[4] Thus heating a mixture of an alkylated product **1** and the appropriate aromatic compound in a 50% aqueous methanolic solution in the presence of concentrated hydrochloric acid gave the desired products **3–6** and **8** in good to excellent yields. Except for **5** and **6b**, all these compounds are novel. Thus this method provides an effective synthesis of certain compounds containing two aromatic rings connected via a methylene bridge.

Regiospecificity in these displacement reactions is controlled both by the electron densities at different positions and by steric hindrance. Reaction of electrophiles at the C-3 (β) position of indole is characteristic of this heterocycle[7] and in the present work gave derivatives **6**. Pyrrole reacts with electrophiles exclusively at the α-position.[8] In our case, both the 2- and 5-positions of pyrrole reacted to

(7) (a) Remers, W. A. *Heterocyclic Compounds, Indole Part 3*; Houlihan, W. J., Ed.; Wiley: New York, 1979; p 357. (b) Ketcha, D. M.; Gribble, G. W. *J. Org. Chem.* **1985**, *50*, 5451.

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Table I. Reaction of 4-(Benzotriazol-1-ylmethyl)anilines with Nucleophiles

entry	R^1	R^2	R	reaction time, h	yield, %	mp, °C	purification solvent
3a	H	-	-	3 d[a]	53	oil	1:2[b]
3b	Me	-	-	3 d	50	oil	benzene[b]
3c	Et	-	-	4 d	68	oil	petroleum ether[c]
4a	H	-	-	57	80	123–124	1:1[b]
4b	Me	-	-	27	73	89–90	8:1[b]
4c	Et	-	-	3 d	72	96–97	hexane[c]
5	-	-	-	7 d	64	141–143[d]	aqueous ethanol[c]
6a	H	H	-	2 d	92	130–132	aqueous MeOH[c]
6b	Me	H	-	7	96	143–145[e]	aqueous MeOH[c]
6c	Et	H	-	3 d	95	134–136	aqueous MeOH[c]
6d	H	Me	-	3 d	85	75–76	2:1[b]
6e	Me	Me	-	20	98	oil	-
6f	Et	Me	-	44	82	oil	18:1[b]
7a	-	-	Ph	6 d	48	oil[f]	40:1[b]
7b	-	-	Me	6 d	36	44–46[g]	12:1[b]
8a	H	H	-	55	29	oil	2:1[b]
8b	Me	H	-	21	52	oil	2:1[b,h]
8c	Et	H	-	5 d	41	72–74	40:1[b]
8d	Me	Me	-	24	45	130–132	40:1[b]
9	-	-	-	27	25	131–133[i]	15:1[j]

[a] d = days. [b] Column chromatography on alumina basic, the ratio indicated petroleum ether (38–56 °C) to ethyl acetate. [c] Recrystallization solvent. [d] Lit.[11] mp 143 °C. [e] Lit.[12] mp 141–144 °C. [f] Lit.[13] mp 51 °C. [g] Lit.[14] mp 47–48 °C. [h] MW 277.1579; found (HRMS) 277.1576. [i] Lit.[11] mp 132–133 °C. [j] Column chromatography on silica gel, the ratio indicated petroleum ether to ethyl acetate.

Table II. Lithiation of 4-(Benzotriazol-1-ylmethyl)-*N,N*-dialkylaniline

substrate	electrophile	products	E	yield, %	mp, °C	solvent
1b	CH_3I	11a	CH_3	99	107–109	MeOH[a]
1b	D_2O	11b	D	90	165–166	MeOH[a]
1b	$PhCH_2Br$	11c	$PhCH_2$	68	147–149	MeOH/EtOAc[a]
1b	p-$CH_3C_6H_4CHO$	11d	p-$CH_3C_6H_4CH(OH)$	50[b] (79[c])	199–201	MeOH[a]
1b	p-$CH_3C_6H_4CHO$	11d′	p-$CH_3C_6H_4CH(OH)$	17[d] (79[c])	187–189	4:1[e]
1b	$Ph_2C{=}O$	11e	$Ph_2C(OH)$	85	202–204	MeOH[a]
1b	$(CH_2)_5C{=}O$	11f	$(CH_2)_5C(OH)$	77	205–207	MeOH[a]
1b	p-$CH_3C_6H_4CO_2Et$	11g	p-$CH_3C_6H_4C(=O)$	62	159–161	61[e,f]
1b	py-4-CHO	11h	py-4-CH(OH)	18[b] (65[c])	218–219	MeOH[a]
1b	py-4-CHO	11h′	py-4-CH(OH)	10[d] (65[c])	190–192	MeOH[a]
1c	CH_3I	11i	CH_3	72	79–81	9:1[g]
1c	$(CH_2)_5C{=}O$	11j	$(CH_2)_5C(OH)$	69	181–183	MeOH[a]
1b	I_2	13	*h*	30	210 dec	6:1[e]

[a] Recrystallization solvent. [b] Isomer I. [c] Total yield of both isomers. [d] Isomer II. [e] Column chromatography on alumina basic, the ratio indicates petroleum ether (38–56 °C) to ethyl acetate. [f] Or trituration with ether. [g] Column chromatography on silica gel, the ratio indicated petroleum ether (38–56 °C) to ethyl acetate. [h] See Scheme I for structure.

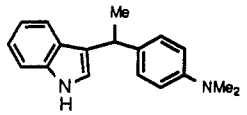
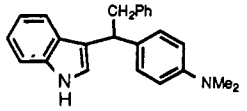
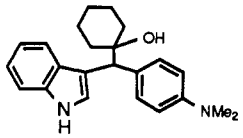
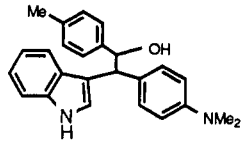
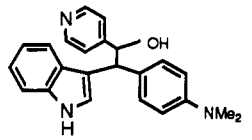
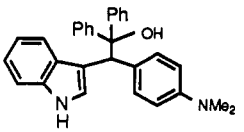
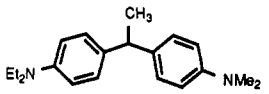
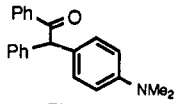
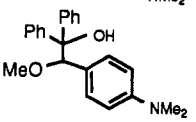
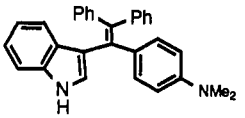
afford products 8. 1,3-Dimethoxybenzene reacted at the less hindered 4-position to give compound 3. 2-Naphthol reacted at the more reactive 1-position forming product 5.

Reactions of 1b with other nucleophiles were also tested, and it was shown to be reactive toward 1,3-dicarbonyl compounds. The product obtained was dependent on the conditions employed. Thus, heating a mixture of 1b with the appropriate 1,3-dicarbonyl compound in 50% aqueous methanol containing concentrated hydrochloric acid under reflux for several days afforded compounds of type 7, where one of the carbonyl groups had been displaced. The properties of compounds thus obtained have been compared to those reported in the literature and structures were further confirmed by their NMR spectra. When the reaction was carried out in an aprotic solvent such as toluene using a Lewis acid catalyst (zinc bromide), product 9 was obtained in 25% yield by direct displacement of benzotriazole.

4-(Benzotriazol-1-ylmethyl)-*N,N*-dimethylaniline (1b) underwent lithiation smoothly with *n*-butyllithium in tetrahydrofuran at −78 °C to form a deep blue solution, which decolorized immediately on addition of 1 equiv of an electrophile, indicating the high reactivity of the anion. When quenched with deuterium oxide, the ^1H NMR spectrum of the compound isolated showed the methylene proton, with a chemical shift similar to that of starting material 1b, but with an integral corresponding to one proton. This indicated that lithiation occurred exclusively at the relatively acidic benzylic methylene carbon. The chelation effect of the dimethylamino group[6] diminishes due to a large acidity difference between the benzene ring proton and a methylene proton α to the strongly electron withdrawing benzotriazole group. Thus we present here a variation on the lithiation of *N,N*-dimethylaniline systems.

Reaction of lithio salt 1b,c with electrophiles such as methyl iodide, benzyl bromide, aldehydes and ketones afforded the desired products 11 in high yields (Scheme I, Table II). With aldehydes, two diastereomeric isomers were obtained. In particular, when *p*-tolualdehyde was used, the diastereomers, obtained in a ratio of 2.5:1, were isolated by repeated recrystallization of the crude product from methanol, followed by column chromatography. With pyridine-4-carboxaldehyde, two isomers, obtained in equal amounts, were isolated similarly. With esters as electrophiles, the yields were low, possibly due to further attack on the products yielding enolate anions. The reaction mixtures in these cases turned dark upon warming to room temperature. Workup at −78 °C did not alter the outcome. With ethyl isonicotinate, a complex mixture was obtained which was not characterized. However, with ethyl *p*-toluate, the expected ketone 11g was obtained in 62% yield. Treatment of the lithio salt with iodine gave 1,2-

Table III. Reactions of Substituted Products 11 with Indole and Aniline

entry	structure	reaction time, h	yield, recryst, % (isolated)	mp, °C
10a		18	91	152–154
10b		40	82	119–121
10c		17	86	162–164
10d		72	38[a]	170–172
10e		20	70	183–185
10f		18	26[b]	211–213
12		4[c]	67	oil
14		18	5[b]	127–129
15		18	9[b]	184–186
16		18	10[b]	209–211

[a] Column on silica gel using petroleum ether/EtOAc = 2:1. [b] Column on silica gel using petroleum ether/EtOAc = 12:1. [c] HOAc was used as the solvent.

bis(4-(*N*,*N*-dimethylamino)phenyl)-1,2-bis(benzotriazol-1-yl)ethane, **13**. Reaction of the lithio derivative of 4-(benzotriazol-1-ylmethyl)-*N*,*N*-diethylaniline (**1c**) with methyl iodide and cyclohexanone afforded the corresponding products **11i,j**, indicating again that lithiation occurred completely at the relatively acidic benzylic methylene carbon.

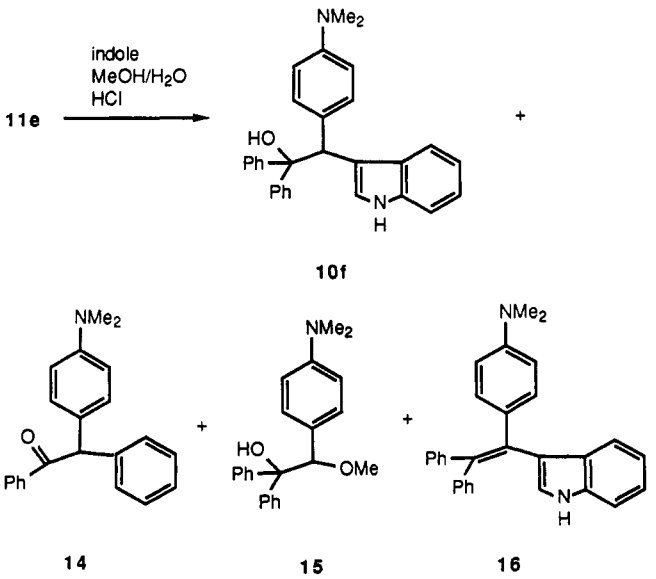
The structures of products **11** were confirmed by their NMR spectra. The methine carbons were observed at 58.7–70.4 ppm (the carbon for **11b** gave a triplet signal at 51.8 ppm). The methine protons usually resonanted between 5.50 and 5.98 ppm except for compound **11g** and **13**. For compound **11g** where the methine carbon was connected to a carbonyl group, the corresponding proton was observed in the aromatic region at 7.78 ppm. For compound **13**, the corresponding methine proton was observed as a singlet at 7.67 ppm indicated by 2D NMR spectra (COSY and HETCOR).

The displacement of benzotriazole from substituted products **11** was also effected by various nucleophiles (Scheme I, Table III). Reaction of **11a** with *N*,*N*-diethylaniline afforded the desired product **12**. Displacement of the benzotriazole group was also accomplished by indole, as evidenced by production of compounds **10a–f** in good yields.

In instances where the electrophile contained a phenyl ring which could possibly migrate, low yields were obtained. With benzophenone derivative **11e**, formation of **10f** in 26% yield was accompanied by the formation of other compounds of which three were isolated and characterized. These arose from the migration of a phenyl group to give ketone **14**, direct displacement of benzotriazole by solvent giving **15**, and dehydration of **10f** to produce **16** (Scheme II). This strengthens our belief that in such reactions, benzotriazole leaves initially forming a relatively stable benzylic cation which can then be trapped by various nucleophiles.

The 4-(*N*,*N*-dimethylanilino) analogues **5** and **6b** have been frequently reported in the literature.[9,10] The literature yields are comparable with those reported in this paper, and some of the other methylene compounds discussed in the present paper could probably also be made by previously reported methods. However, these methods are strictly restricted to compounds with a $-CH_2-$ linkage, and no previous examples are known for a –CHX– linkage. It is for such –CHX– derivatives that our method is uniquely valuable since products of type **10** and **12** can be readily prepared.

Scheme II



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(14) Finkelstein, J.; Romano, J. A.; Chiang, E.; Lee, J. *J. Med. Chem.* **1963**, *6*, 153.

The structures of derivatives 3–6, 8, 10, and 12 were confirmed by their spectral data and elemental analyses. Methylene protons appeared in the region 3.73–4.33 ppm (and 3.99–4.49 ppm for the methine protons) and, in the ^{13}C NMR, the corresponding methylene carbon resonanted in the region 27.0–34.1 ppm (and between 35.8–51.3 ppm for the methine carbon). The upfield shift of the methine signals in both ^{1}H and ^{13}C NMR spectra indicated loss of an electron-withdrawing group directly attached to it. This, coupled with the absence of benzotriazole resonances, confirmed that displacement of the benzotriazole had occurred.

In summary, 4-(benzotriazol-1-ylmethyl)-*N*,*N*-dialkylanilines undergo smooth lithiation at the methylene carbon. Displacement of benzotriazole from the parent compounds or their substituted products by benzenoid and heteroaromatic nucleophiles led to a series of novel, unsymmetrical, di- or trisubstituted methanes. Selection of appropriate fragments could lead to compounds with potential applications as dyestuffs (due to the extended conjugation) and in synthesis.

Experimental Section

General. Tetrahydrofuran (THF) was distilled from sodium/benzophenone immediately prior to use. Electrophiles were purified by standard methods before use. Lithiation reactions were performed in oven-dried glassware under a nitrogen atmosphere. Column chromatography was carried out using alumina basic (Brockman Activity I, 80–200 mesh) or MBS silica gel (230–400 mesh) as indicated. Melting points were measured in a Thomas-Hoover melting point apparatus and are uncorrected. ^{1}H NMR (300 MHz) and ^{13}C NMR (75 MHz) spectra were measured on a Varian VXR-300 spectrometer in $CDCl_3$ solutions. For ^{1}H NMR spectra, multiplicity is denoted by s (singlet), d (doublet), t (triplet), m (multiplet), and br (broad). Coupling constants are in hertz. Mass spectra were recorded on a AEI MS 30 mass spectrometer. Exact mass measurements were performed on a KRATOS MS-80-RFA double-focusing spectrometer using the peak matching technique at a nominal resolution of 5000 (10% valley definition). Elemental analyses (C, H, N) were carried out using a Carbo Erba 1106 elemental analyzer under the supervision of Dr. D. Powell at the University of Florida.

Compounds 1a–c were prepared according to the literature procedures.[4]

Displacement of Benzotriazole by Nucleophiles. General Procedure. To a stirred solution of the corresponding (benzotriazol-1-ylmethyl)aniline 1 (5 mmol) in MeOH (30 mL) under reflux was added a solution of the appropriate nucleophile (5 mmol) and concentrated hydrochloric acid (1 mL) in water (30 mL). The resulting mixture was heated under reflux for the appropriate time followed by addition of an aqueous KOH solution (1 M; 50 mL) and subsequently cooled. The products were isolated either by filtration or by extraction into ether and were purified by recrystallization or by column chromatography. The melting points of the products and purifying solvents are presented in Table I.

2-((4-Aminophenyl)methyl)-1,5-dimethoxybenzene (3a): ^{1}H NMR δ 3.42 (s, br, 2 H), 3.73 (s, br, 6 H), 3.77 (s, 2 H), 6.3–6.4 (m, 2 H), 6.5–6.6 (m, 2 H), 6.90–6.97 (m, 3 H); ^{13}C NMR δ 34.1, 55.12, 55,15, 98.3, 103.7, 115.0, 122.7, 129.5, 130.2, 131.1, 144.1, 158.0, 159.0. Anal. Calcd for $C_{15}H_{17}NO_2$: C, 74.05; H, 7.04. Found: C, 74.33; H, 7.09.

2-((4-(*N*,*N*-Dimethylamino)phenyl)methyl)-1,5-dimethoxybenzene (3b): ^{1}H NMR δ 2.87 (s, 6 H), 3.74 (s, 3 H), 3.76 (s, 3 H), 3.80 (s, 2 H), 6.3–6.7 (m, 4 H), 6.92 (d, 1 H, J = 8), 7.0–7.1 (m, 2 H); ^{13}C NMR δ 34.0, 40.8, 55.2, 55.3, 98.4, 103.8, 112.9, 122.9, 129.4, 129.5, 130.2, 148.9, 158.1, 159.1. Anal. Calcd for $C_{17}H_{21}NO_2$: C, 75.25; H, 7.80. Found: C, 75.42; H, 7.82.

2-((4-(*N*,*N*-Diethylamino)phenyl)methyl)-1,5-dimethoxybenzene (3c): ^{1}H NMR δ 1.09 (t, 6 H, J = 7), 3.25 (q, 4 H, J = 7), 3.70 (s, 3 H), 3.73 (s, 3 H), 3.78 (s, 2 H), 6.35 (dd, 1 H, J = 8, 2), 6.41 (d, 2 H, J = 2), 6.58 (d, 2 H, J = 8.8), 6.93 (d, 1 H, J = 8), 7.02 (d, 2 H, J = 8.8); ^{13}C NMR δ 12.5, 33.9, 44.3, 55.06, 55.11, 98.3, 103.7, 112.0, 123.0, 128.1, 129.5, 130.2, 145.9, 158.0, 159.0. Anal. Calcd for $C_{19}H_{25}NO_2$: C, 76.22; H, 8.42. Found: C, 76.00; H, 8.45.

2-((4-Aminophenyl)methyl)-1,3,5-trimethoxybenzene (4a): ^{1}H NMR δ 3.75 (s, 6 H), 3.77 (s, 3 H), 3.81 (s, 2 H), 6.12 (s, 2 H), 6.51–6.54 (m, 2 H), 7.01 (d, 2 H, J = 8.5); ^{13}C NMR δ 27.2, 55.2, 55.6, 90.5, 110.8, 115.0, 129.1, 132.3, 143.7, 158.7, 159.3. Anal. Calcd for $C_{16}H_{19}NO_3$: C, 70.31; H, 7.01; N, 5.12. Found: C, 70.55; H, 7.11; N, 5.01.

2-((4-(*N*,*N*-Dimethylamino)phenyl)methyl)-1,3,5-trimethoxybenzene (4b): ^{1}H NMR δ 2.81 (s, 6 H), 3.73 (s, 9 H), 3.83 (s, 2 H), 6.10 (s, 2 H), 6.60 (d, 2 H, J = 8.6), 7.10 (d, 2 H, J = 8); ^{13}C NMR δ 27.0, 40.8, 55.0, 55.4, 90.4, 110.8, 112.8, 128.8, 130.5, 148.6, 158.6, 159.3. Anal. Calcd for $C_{18}H_{23}NO_3$: C, 71.73; H, 7.69; N, 4.65. Found: C, 71.45; H, 7.75; N, 4.63.

2-((4-(*N*,*N*-Diethylamino)phenyl)methyl)-1,3,5-trimethoxybenzene (4c): ^{1}H NMR δ 1.09 (t, 6 H, J = 7), 3.26 (q, 4 H, J = 7), 3.77 (s, 6 H), 3.78 (s, 3 H), 3.81 (s, 2 H), 6.13 (s, 2 H), 6.56 (d, 2 H, J = 8.8), 7.08 (d, 2 H, J = 8.8); ^{13}C NMR δ 12.6, 27.0, 44.4, 55.3, 55.6, 90.6, 111.2, 112.1, 129.1, 129.3, 145.7, 158.7, 159.3. Anal. Calcd for $C_{20}H_{27}NO_3$: C, 72.92; H, 8.26; N, 4.25. Found: C, 72.82; H, 8.37; N, 4.19.

1-((4-(*N*,*N*-Dimethylamino)phenyl)methyl)-2-naphthol (5): ^{1}H NMR δ 2.84 (s, 6 H), 4.33 (s, 2 H), 5.40 (s, br, 1 H), 6.62–6.65 (m, 2 H), 7.06 (dd, 3 H, J = 8.7, 3), 7.29 (dt, 1 H, J = 8, 1), 7.42 (dt, 1 H, J = 8, 1), 7.64 (d, 1 H, J = 8.8), 7.76 (d, 1 H, J = 8), 7.94 (d, 1 H, J = 8.5); ^{13}C NMR δ 29.7, 40.9, 113.3, 118.0, 118.7, 123.0, 123.3, 126.5, 127.7, 128.2, 128.4, 128.8, 129.4, 133.6, 149.3, 151.4.

3-((4-Aminophenyl)methyl)indole (6a): ^{1}H NMR δ 3.51 (s, br, 2 H), 3.99 (s, 2 H), 6.57–6.61 (m, 2 H), 6.81–6.82 (m, 1 H), 7.0–7.3 (m, 5 H), 7.50 (d, 1 H, J = 8), 7.87 (s, br, 1 H); ^{13}C NMR δ 30.7, 111.0, 115.2, 116.4, 119.2, 119.3, 121.8, 122.2, 127.4, 129.4, 131.3, 136.4, 144.2. Anal. Calcd for $C_{15}H_{14}N_2$: C, 81.05; H, 6.35; N, 12.60. Found: C, 80.91; H, 6.39; N, 12.44.

3-((4-(*N*,*N*-Dimethylamino)phenyl)methyl)indole (6b): ^{1}H NMR δ 2.89 (s, 6 H), 4.01 (s, 2 H), 6.68 (d, 2 H, J = 8), 6.82 (s, 1 H), 7.06 (t, 2 H, J = 7.7), 7.14–7.30 (m, 3 H), 7.53 (d, 1 H, J = 8), 7.85 (s, br, 1 H); ^{13}C NMR δ 30.5, 40.9, 110.9, 113.0, 116.6, 119.1, 119.2, 121.8, 122.1, 127.5, 129.2, 129.4, 136.4, 149.0.

3-((4-(*N*,*N*-Diethylamino)phenyl)methyl)indole (6c): ^{1}H NMR δ 1.10 (t, 6 H, J = 7), 3.27 (q, 4 H, J = 7), 3.98 (s, 2 H), 6.60 (d, 2 H, J = 8.5), 6.75 (d, 1 H, J = 1.2), 7.0–7.2 (m, 5 H), 7.54 (d, 1 H, J = 8), 7.69 (s, br, 1 H); ^{13}C NMR δ 12.5, 30.3, 44.4, 111.0, 112.2, 116.5, 119.0, 119.1, 121.7, 122.2, 127.5, 128.2, 129.4, 136.3, 146.1. Anal. Calcd for $C_{19}H_{22}N_2$: C, 81.97; H, 7.97; N, 10.06. Found: C, 81.77; H, 8.05; N, 10.09.

3-((4-Aminophenyl)methyl)-*N*-methylindole (6d): ^{1}H NMR δ 3.40 (s, br, 2 H), 3.57 (s, 3 H), 3.95 (s, 2 H), 6.51 (dt, 2 H, J = 8, 2), 6.64 (s, 1 H), 7.00–7.06 (m, 3 H), 7.13–7.23 (m, 2 H), 7.49 (dt, 1 H, J = 8, 1); ^{13}C NMR δ 30.5, 32.3, 108.9, 114.9, 115.0, 118.5, 119.1, 121.3, 126.8, 127.7, 129.3, 131.2, 137.0, 144.2. Anal. Calcd for $C_{16}H_{16}N_2$: C, 81.32; H, 6.82; N, 11.85. Found: C, 81.66; H, 6.95; N, 11.87.

3-((4-(*N*,*N*-Dimethylamino)phenyl)methyl)-*N*-methylindole (6e): ^{1}H NMR δ 2.81 (s, 6 H), 3.52 (s, 3 H), 3.95 (s, 2 H), 6.60–6.66 (m, 3 H), 7.0–7.2 (m, 5 H), 7.51 (dt, 1 H, J = 8, 1); ^{13}C NMR δ 30.3, 32.3, 40.7, 108.9, 112.8, 115.0, 118.5, 119.1, 121.3, 126.8, 127.8, 129.1, 129.4, 137.0, 148.9. Anal. Calcd for $C_{18}H_{20}N_2$: C, 81.78; H, 7.63; N, 10.60. Found: C, 82.01; H, 7.92; N, 10.63.

3-((4-(*N*,*N*-Diethylamino)phenyl)methyl)-*N*-methylindole (6f): ^{1}H NMR δ 1.09 (t, 6 H, J = 7), 3.25 (q, 4 H, J = 7), 3.57 (s, 3 H), 3.97 (s, 2 H), 6.59 (dt, 2 H, J = 8.7, 2), 6.85 (s, 1 H), 7.01–7.23 (m, 5 H), 7.54 (dt, 1 H, J = 8, 1); ^{13}C NMR δ 12.5, 30.3, 32.3, 44.3, 108.9, 112.1, 115.2, 118.5, 119.2, 121.3, 126.8, 127.9, 128.2, 129.3, 137.0, 146.0. Anal. Calcd for $C_{20}H_{24}N_2$: C, 82.15; H, 8.27; N, 9.58. Found: C, 82.03; H, 8.39; N, 9.47.

3-(4-(*N*,*N*-Dimethylamino)phenyl)propiophenone (7a): ^{1}H NMR δ 2.86 (s, 6 H), 2.95 (t, 2 H, J = 8), 3.21 (t, 2 H, J = 8), 6.67 (d, 2 H, J = 8.8), 7.11 (d, 2 H, J = 8.8), 7.35–7.50 (m, 3 H), 7.91–7.94 (m, 2 H); ^{13}C NMR δ 29.1, 40.6, 40.7, 112.9, 127.9, 128.4, 128.8, 129.1, 132.7, 136.8, 149.0, 199.4.

4-(4-(*N*,*N*-Dimethylamino)phenyl)-2-butanone (7b): ^{1}H NMR δ 2.12 (s, 3 H), 2.65–2.82 (m, 4 H), 2.90 (s, 6 H), 6.68 (d, 2 H, J = 8.7), 7.05 (d, 2 H, J = 8.7); ^{13}C NMR δ 28.8, 30.0, 40.8, 45.6, 112.9, 128.8, 128.9, 149.1, 208.5.

2,5-Bis((4-aminophenyl)methyl)pyrrole (8a): ^{1}H NMR δ 3.46 (s, br, 4 H), 3.73 (s, 4 H), 5.78 (d, 2 H, J = 2.6), 6.53–6.56 (m, 4 H), 6.90–6.94 (m, 4 H), 7.58 (s, br, 1 H); ^{13}C NMR δ 33.1, 105.9, 115.2, 129.3, 129.6, 130.6, 144.5; HRMS calcd for $C_{18}H_{19}N_3$ m/z 277.1579, found 277.1576.

2,5-Bis((4-(*N*,*N*-dimethylamino)phenyl)methyl)pyrrole (8b): ^{1}H NMR δ 2.85 (s, 12 H), 3.73 (s, 4 H), 5.78 (d, 2 H, J = 2.6), 6.62–6.65 (m, 4 H), 7.00–7.03 (m, 4 H), 7.45 (s, br, 1 H); ^{13}C NMR δ 32.9, 40.7, 105.8, 112.8, 127.7, 129.1, 130.6, 149.1. Anal. Calcd for $C_{22}H_{27}N_3$: C, 79.24; H, 8.16. Found: C, 79.06; H, 8.11.

2,5-Bis((4-(*N*,*N*-diethylamino)phenyl)methyl)pyrrole (8c): ^{1}H NMR δ 1.13 (t, 12 H, J = 7), 3.26 (q, 8 H, J = 7), 3.77 (s, 4 H), 5.81 (d, 2 H, J = 2.6), 6.59–6.62 (m, 4 H), 7.00–7.03 (m, 4 H), 7.48 (s, br, 1 H); ^{13}C NMR δ 12.5, 33.0, 44.4, 105.8, 112.1, 126.5, 129.4, 130.8, 146.3. Anal. Calcd for $C_{28}C_{35}N_3$: C, 80.16; H, 9.06; N, 10.79. Found: C, 79.79; H, 9.21; N, 10.55.

2,5-Bis((4-(*N*,*N*-dimethylamino)phenyl)methyl)-*N*-methylpyrrole (8d): ^{1}H NMR δ 2.88 (s, 12 H), 3.19 (s, 3 H), 3.80 (s, 4 H), 5.78 (s, 2 H), 6.47 (d, 4 H, J = 8.8), 7.01 (d, 4 H, J = 8.8); ^{13}C NMR δ 30.4, 32.3, 40.8, 105.9, 112.8, 127.5, 129.0, 131.8, 149.1. Anal. Calcd for $C_{23}H_{29}N_3$: C, 79.50; H, 8.41; N, 12.09. Found: C, 79.51; H, 8.61; N, 12.14.

Preparation of Substituted 4-(Benzotriazol-1-ylmethyl)anilines (11a–j). General Procedure. To a solution of the substrate (2.5 mmol) in THF (80 mL) at −78 °C was added dropwise *n*-BuLi (2.5 M in hexane; 1.0 mL, 2.5 mmol). The mixture was stirred at −78 °C for 2 h, and then a solution of the appropriate electrophile (2.5 mmol) in THF (5 mL) was added slowly. The mixture was kept at −78 °C for a few hours and allowed to warm to room temperature overnight. Water (30 mL) was added to quench the reaction, and the solution was extracted with ether. The combined ether extracts were washed with water and dried over $MgSO_4$. The solvent was removed under reduced pressure, and the residue was purified by recrystallization or by column chromatography. The melting points of the products and purifying solvents are presented in Table II.

4-(1-(Benzotriazol-1-yl)ethyl)-*N*,*N*-dimethylaniline (11a): ^{1}H NMR δ 2.10 (d, 3 H, J = 7), 2.89 (s, 6 H), 5.98 (q, 1 H, J = 7), 6.63 (d, 2 H, J = 8.8), 7.17 (d, 2 H, J = 8.8), 7.24–7.30 (m, 3 H), 8.00–8.04 (m, 1 H); ^{13}C NMR δ 20.9, 40.3, 58.7, 110.4, 112.2, 119.7, 123.5, 126.6, 127.20, 127.24, 132.2, 146.3, 150.1. Anal. Calcd for $C_{16}H_{18}N_4$: C, 72.15; H, 6.81; N, 21.04. Found: C, 72.32; H, 6.92; N, 21.28.

(Benzotriazol-1-yl)(4-(*N*,*N*-dimethylamino)phenyl)-deuteriomethane (11b): ^{1}H NMR δ 2.89 (s, 6 H), 5.70 (s, 1 H), 6.62–6.65 (m, 2 H), 7.18–7.37 (m, 5 H), 8.00–8.03 (m, 1 H); ^{13}C NMR δ 40.3, 51.8 (t, J = 21), 110.0, 112.3, 119.8, 121.8, 123.6, 127.0, 128.8, 132.6, 146.3, 150.4; HRMS calcd for $C_{15}H_{16}DN_4$ m/z 253.1437, found 253.1423.

4-(1-(Benzotriazol-1-yl)-1-benzylmethyl)-*N*,*N*-dimethylaniline (11c): ^{1}H NMR δ 2.88 (s, 6 H), 3.70 (dd, 1 H, J = 6.4, 14.0), 4.07 (dd, 1 H, J = 8.8, 14.0), 5.90 (dd, 1 H, J = 6.4, 8.8), 6.61 (d, 2 H, J = 8.8), 7.03–7.30 (m, 10 H), 7.95–7.99 (m, 1 H); ^{13}C NMR δ 40.3, 41.2, 64.9, 109.8, 112.2, 119.7, 123.5, 126.1, 126.5, 126.8, 127.8, 128.3, 129.0, 132.7, 137.5, 146.0, 150.2. Anal. Calcd for $C_{22}H_{22}N_4$: C, 77.16; H, 6.48; N, 16.36. Found: C, 77.15; H, 6.52; N, 16.64.

1-(4-Tolyl)-2-(benzotriazol-1-yl)-2-(4-(dimethylamino)-phenyl)ethanol. Isomer I (11d): ^{1}H NMR δ 2.26 (s, 3 H), 2.80 (s, 6 H), 4.12 (d, 1 H, J = 4), 5.72 (d, 1 H, J = 8.8), 5.89 (dd, 1 H, J = 4, 8.8), 6.44 (d, 2 H, J = 8.8), 6.94 (d, 2 H, J = 8.8), 7.01 (d, 2 H, J = 8), 7.12 (d, 2 H, J = 8), 7.21–7.35 (m, 3 H), 7.96 (d, 1 H, J = 8); ^{13}C NMR δ 21.1, 40.1, 70.0, 76.0, 110.2, 111.9, 119.5, 123.3, 123.9, 126.9, 127.2, 128.4, 128.8, 133.5, 136.7, 137.3, 145.6, 150.0. Anal. Calcd for $C_{23}H_{24}N_4O$: C, 74.17; H, 6.49; N, 15.04. Found: C, 73.86; H, 6.57; N, 15.12.

Isomer II (11d′): ^{1}H NMR δ 2.22 (s, 3 H), 2.88 (s, 6 H), 3.65 (s, br, 1 H), 5.65 (d, 1 H, J = 6), 5.93 (d, 1 H, J = 6), 6.57–6.60 (m, 2 H), 6.96–6.98 (m, 2 H), 7.12–7.26 (m, 7 H), 7.92–7.96 (m, 1 H); ^{13}C NMR δ 21.0, 40.2, 68.8, 75.0, 109.7, 111.9, 119.6, 122.0, 123.8, 126.5, 127.1, 128.7, 129.4, 132.9, 136.8, 137.4, 145.2, 150.4. Anal. Calcd for $C_{23}H_{24}N_4O$: C, 74.17; H, 6.49; N, 15.04. Found: C, 74.06; H, 6.69; N, 14.80.

2-(Benzotriazol-1-yl)-2-(4-(dimethylamino)phenyl)-1,1-diphenylethanol (11e): ^{1}H NMR δ 1.65 (s, 1 H), 2.81 (s, 6 H), 5.83 (s, 1 H), 6.39–6.41 (m, 2 H), 6.55 (s, 1 H), 6.84–6.87 (m, 2 H), 7.00–7.55 (m, 12 H), 7.96 (d, 1 H, J = 8); ^{13}C NMR δ 40.2, 68.2, 81.4, 109.5, 111.3, 120.0, 122.1, 124.2, 125.5, 126.5, 126.8, 126.9, 127.7, 127.8, 128.2, 129.7, 133.2, 143.3, 144.8, 145.7, 149.8. Anal. Calcd for $C_{28}H_{26}N_4O$: C, 77.39; H, 6.03; N, 12.89. Found: C, 77.01; H, 6.06; N, 12.97.

1-((Benzotriazol-1-yl)(4-(dimethylamino)phenyl)-methyl)cyclohexan-1-ol (11f): ^{1}H NMR δ 1.20–1.66 (m, 10 H), 2.88 (s, 6 H), 4.01 (s, 1 H), 5.50 (s, 1 H), 6.62 (d, 2 H, J = 8.8), 7.26–7.53 (m, 5 H), 8.03 (d, 1 H, J = 8); ^{13}C NMR δ 21.5, 21.8, 25.5, 35.0, 36.1, 40.2, 70.4, 74.3, 109.8, 111.8, 119.8, 122.8, 124.1, 127.5, 129.8, 133.8, 144.9, 150.3. Anal. Calcd for $C_{21}H_{26}N_4O$: C, 71.97; H, 7.48; N, 15.99. Found: C, 71.89; H, 7.51; N, 16.37.

2-(Benzotriazol-1-yl)-2-(4-(dimethylamino)phenyl)-4′-methylacetophenone (11g): ^{1}H NMR δ 2.32 (s, 3 H), 2.87 (s, 6 H), 6.61 (d, 2 H, J = 8.8), 7.17–7.30 (m, 7 H), 7.78 (s, 1 H), 7.91–8.00 (m, 3 H); ^{13}C NMR δ 21.5, 39.8, 68.3, 111.8, 112.1, 119.1, 119.5, 123.4, 127.0, 129.0, 129.4, 130.2, 131.9, 133.3, 144.8, 146.4, 150.5, 192.7. Anal. Calcd for $C_{23}H_{22}N_4O$: C, 74.57; H, 5.99; N, 15.12. Found: C, 74.60; H, 6.17; N, 15.14.

2-(Benzotriazol-1-yl)-2-(4-(dimethylamino)phenyl)-1-(pyrid-4-yl)ethanol. Isomer I (11h): ^{1}H NMR δ 2.00 (s, br, 1 H), 2.87 (s, 6 H), 5.61 (d, 1 H, J = 8), 5.93 (d, 1 H, J = 8.8), 6.48 (d, 2 H, J = 8), 6.90 (d, 2 H, J = 8), 7.11 (d, 2 H, J = 5), 7.3–7.4 (m, 3 H), 8.00 (d, 1 H, J = 8), 8.41 (d, 2 H, J = 5); ^{13}C NMR δ 40.1, 69.8, 75.2, 110.1, 112.0, 119.8, 122.1, 122.2, 124.3, 127.6, 128.4, 133.4, 145.7, 148.8, 149.4, 150.4. Anal. Calcd for $C_{21}H_{21}N_5O$: C, 70,18; H, 5.89; N, 19.48. Found: C, 69.94; H, 5.94; N, 19.54.

Isomer II (11h′): ^{1}H NMR δ 2.88 (s, 6 H), 4.90 (s, br, 1 H), 5.63 (d, 1 H, J = 6), 5.98 (d, 1 H, J = 6), 6.55 (d, 2 H, J = 8.8), 7.1–7.3 (m, 7 H), 7.96 (d, 1 H, J = 7), 8.30 (d, 2 H, J = 3); ^{13}C NMR δ 40.1, 68.3, 73.8, 109.7, 110.8, 119.7, 121.1, 121.7, 124.1, 127.4, 129.4, 132.9, 145.3, 149.2, 149.4, 150.5. Anal. Calcd for $C_{21}H_{21}N_5O$: C, 70.18; H, 5.89; N, 19.48. Found: C, 70.30; H, 5.91; N. 19.72.

4-(1-(Benzotriazol-1-yl)ethyl)-*N*,*N*-diethylaniline (11i): ^{1}H NMR δ 1.10 (t, 6 H, J = 7), 2.10 (d, 3 H, J = 7), 3.28 (q, 4 H, J = 7), 5.96 (q, 1 H, J = 7), 6.57 (d, 2 H, J = 8.8), 7.15 (d, 2 H, J = 8.8), 7.23–7.30 (m, 3 H), 8.00 (d, 1 H, J = 8); ^{13}C NMR δ 12.4, 20.9, 44.1, 58.7, 110.5, 111.5, 119.6, 123.4, 126.1, 126.5, 127.5, 132.2, 146.3, 147.5. Anal. Calcd for $C_{18}H_{22}N_4$: C, 73.44; H, 7.53; N, 19.03. Found: C, 73.16; H, 7.67; N, 19.08.

1-((Benzotriazol-1-yl)(4-(*N*,*N*-diethylamino)phenyl)-methyl)cyclohexan-1-ol (11j): ^{1}H NMR δ 1.08 (t, 6 H, J =7), 1.2–1.8 (m, 10 H), 3.26 (q, 4 H, J = 7), 4.02 (s, 1 H), 5.50 (s, 1 H), 6.55 (d, 2 H, J = 8), 7.3–7.6 (m, 5 H), 8.03 (d, 1 H, J = 8); ^{13}C NMR δ 12.4, 21.5, 21.7, 25.5, 34.9, 36.0, 44.0, 70.4, 74.3, 109.8, 110.8, 119.7, 121.4, 124.0, 127.3, 130.0, 133.7, 144.8, 147.5. Anal. Calcd for $C_{23}H_{30}N_4O$: C, 72.98; H, 7.99; N, 14.80. Found: C, 72.71; H, 8.14; N, 14.96.

1,2-Bis(4-(*N*,*N*-dimethylamino)phenyl)-1,2-bis(benzotriazol-1-yl)ethane (13). To a solution of 4-(benzotriazol-1-ylmethyl)-*N*,*N*-dimethylaniline (1.26 g, 5 mmol) in THF (160 mL) at −78 °C was added *n*-BuLi (2.5 M in hexane; 2.0 mL, 5 mmol) via a syringe under nitrogen. The mixture was stirred at −78 °C for 1 h, and then a solution of iodine (1.4 g) in THF (10 mL) was added. The whole was stirred at −78 °C for 2 h, and water (30 mL) was added at −78 °C. The resultant mixture was allowed to warm to room temperature overnight and extracted with methylene chloride. The organic layer was washed with saturated sodium thiosulfate solution (150 mL) and dried ($MgSO_4$). Evaporation of solvent gave a black residue, which was purified to give the desired product (0.38 g, 30%): ^{1}H NMR δ 2.77 (s, 12 H), 6.56 (d, 4 H, J = 8.8), 7.28 (t, 2 H, J = 8), 7.53 (t, 2 H, J = 8), 7.67 (s, 2 H), 7.72 (d, 4 H, J = 8.8), 7.80 (d, 2 H, J = 8), 8.34 (d, 2 H, J = 8); ^{13}C NMR δ 39.7, 63.3, 111.1, 111.7, 118.7, 123.2, 124.0, 127.1, 129.3, 132.5, 144.5, 149.9. Anal. Calcd for $C_{30}H_{30}N_8$: C, 71.69; H, 6.02; N, 22.29. Found: C, 71.50; H, 6.02; N, 22.54.

Displacement of Benzotriazole from Substituted 4-(Benzotriazol-1-ylmethyl)anilines. General Procedure. To a stirred solution of the corresponding substituted (benzotriazol-1-ylmethyl)aniline 11 (5 mmol) in MeOH (30 mL) under reflux was added a solution of the appropriate nucleophile (5 mmol) and concentrated hydrochloric acid (1 mL) in water (30 mL). The resulting mixture was heated under reflux for the appropriate time followed by addition of an aqueous KOH solution (1 M; 50 mL) and subsequently cooled. The products were isolated either by filtration or by extraction into ether and were purified

by recrystallization or by column chromatography. The melting points of the products and purifying solvents are presented in Table III.

3-(1-(4-(*N*,*N*-Dimethylamino)phenyl)ethyl)indole (10a): ^{1}H NMR δ 1.65 (d, 3 H, *J* = 7), 2.87 (s, 6 H), 4.28 (q, 1 H, *J* = 7), 6.67 (d, 2 H, *J* = 8.5), 6.89–7.41 (m, 7 H), 7.82 (s, br, 1 H); ^{13}C NMR δ 22.5, 35.8, 40.8, 110.9, 112.9, 119.0, 119.8, 120.9, 121.7, 122.1, 126.9, 128.0, 135.1, 136.6, 148.9. Anal. Calcd for $C_{18}H_{20}N_2$: C, 81.78; H, 7.63; N, 10.60. Found: C, 81.54; H, 7.66; N, 10.75.

4-(Benzyl(indol-3-yl)methyl)-*N*,*N*-dimethylaniline (10b): ^{1}H NMR δ 2.82 (s, 6 H), 3.24 (dd, 1 H, *J* = 8.4, 13.6), 3.46 (dd, 1 H, *J* = 13.6, 6.8), 4.39 (dd, 1 H, *J* = 8.4, 6.8), 6.59 (d, 2 H, *J* = 8.5), 6.86–7.43 (m, 12 H), 7.71 (s, br, 1 H); ^{13}C NMR δ 40.7, 42.6, 43.7, 110.9, 112.7, 119.0, 119.6, 120.2, 121.4, 121.7, 125.6, 126.9, 127.9, 128.6, 129.0, 132.7, 136.4, 141.0, 148.9. Anal. Calcd for $C_{24}H_{24}N_2$: C, 84.67; H, 7.11; N, 8.23. Found: C, 84.65; H, 7.17; N, 8.00.

1-((4-(*N*,*N*-Dimethylamino)phenyl)(indol-3-yl)methyl)-cyclohexan-1-ol (10c): ^{1}H NMR δ 1.20–1.72 (m, 10 H), 2.86 (s, 6 H), 4.21 (s, 1 H), 6.65 (d, 2 H, *J* = 8.5), 7.03–7.43 (m, 7 H), 7.62 (d, 1 H, *J* = 8), 8.09 (s, br, 1 H); ^{13}C NMR δ 22.3, 25.8, 36.7, 37.0, 40.7, 51.3, 73.9, 110.8, 112.5, 116.5, 118.9, 119.1, 121.6, 122.4, 128.4, 129.9, 130.1, 135.4, 149.1. Anal. Calcd for $C_{23}H_{28}N_2O$: C, 79.27; H, 8.10; N, 8.04. Found: C, 79.27; H, 8.07; N, 8.39.

1-(4-Tolyl)-2-(4-(*N*,*N*-dimethylamino)phenyl)-2-(indol-3-yl)ethanol (10d): ^{1}H NMR δ 2.26 (s, 3 H), 2.45 (s, br, 1 H), 2.81 (s, 6 H), 4.49 (d, 1 H, *J* = 8), 5.25 (d, 1 H, *J* = 8), 6.52 (d, 2 H, *J* = 8.8), 6.9–7.3 (m, 10 H), 7.47 (d, 1 H, *J* = 8), 8.10 (s, br, 1 H); ^{13}C NMR δ 21.1, 40.6, 50.7, 77.5, 111.0, 112.5, 115.8, 119.3, 119.5, 122.0, 122.4, 126.7, 127.6, 128.5, 129.2, 130.0, 136.3, 136.5, 139.7, 149.0. Anal. Calcd for $C_{25}H_{26}N_2O$: C, 81.05; H, 7.07; N, 7.56. Found: C, 80.81; H, 7.13; N, 7.43.

1-(Pyrid-4-yl)-2-(4-(*N*,*N*-dimethylamino)phenyl)-2-(indol-3-yl)ethanol (10e): ^{1}H NMR δ 2.72 (s, br, 1 H), 2.86 (s, 6 H), 4.47 (d, 1 H, *J* = 7), 5.28 (d, 1 H, *J* = 7), 6.56 (d, 2 H, *J* = 8.8), 7.01–7.33 (m, 10 H), 7.43 (d, 1 H, *J* = 7.6), 8.28 (s, br, 1 H), 8.40 (d, 2 H, *J* = 6); ^{13}C NMR δ 40.6, 50.5, 76.5, 111.1, 112.6, 114.7, 119.3, 119.7, 121.7, 122.5, 127.4, 128.6, 129.2, 136.3, 149.2, 149.4, 151.7. Anal. Calcd for $C_{23}H_{23}N_3O$: C, 77.28; H, 6.49; N, 11.76. Found: C, 77.04; H, 6.64; N, 11.63.

2-(4-(*N*,*N*-Dimethylamino)phenyl)-2-(indol-3-yl)-1,1-diphenylethanol (10f): ^{1}H NMR δ 2.74 (s, 6 H), 3.03 (s, 1 H), 5.43 (s, 1 H), 6.38 (d, 2 H, *J* = 8.6), 6.77–7.32 (m, 16 H), 7.49 (d, 1 H, H, *J* = 7.4), 7.73 (s, br, 1 H); ^{13}C NMR δ 40.4, 50.6, 81.0, 110.7, 112.1, 115.3, 118.9, 119.0, 121.4, 125.0, 125.7, 125.9, 126.0, 126.3, 127.3, 127.6, 127.7, 130.6, 135.4, 146.5, 147.6, 149.0. Anal. Calcd for $C_{30}H_{28}N_2O$: C, 83.30; H, 6.52; N, 6.48. Found: C, 83.04; H, 6.62; N, 6.29.

1-(4-(*N*,*N*-Dimethylamino)phenyl)-1-(4-(*N*,*N*-diethylamino)phenyl)ethane (12): ^{1}H NMR δ 1.12 (t, 6 H, *J* = 7), 1.55 (d, 3 H, *J* = 7), 2.88 (s, 6 H), 3.29 (q, 4 H, *J* = 7), 3.96 (q, 1 H, *J* = 7), 6.60 (d, 2 H, *J* = 8.8), 6.67 (d, 2 H, *J* = 8.8), 7.05 (d, 2 H, *J* = 8.8), 7.10 (d, 2 H, *J* = 8.8); ^{13}C NMR δ 12.6, 22.3, 40.9, 42.7, 44.3, 111.9, 112.8, 128.1, 128.2, 134.1, 135.7, 146.0, 148.9. Anal. Calcd for $C_{20}H_{28}N_2$: C, 81.03; H, 9.52. Found: C, 81.44; H, 9.74.

2-Phenyl-2-(4-(*N*,*N*-dimethylamino)phenyl)acetophenone (14): ^{1}H NMR δ 2.90 (s, 6 H), 5.93 (s, 1 H), 6.68 (d, 2 H, *J* = 8.8), 7.1–7.5 (m, 10 H), 8.00–8.02 (m, 2 H); ^{13}C NMR δ 40.5, 58.6, 112.8, 126.5, 126.8, 128.48, 128.5, 128.9, 129.1, 129.8, 132.7, 137.1, 140.0, 149.6, 198.7. Anal. Calcd for $C_{22}H_{21}NO$: C, 83.78; H, 6.71; N, 4.44. Found: C, 83.41; H, 6.86; N, 4.35.

2-(4-(*N*,*N*-Dimethylamino)phenyl)-2-methoxy-1,1-diphenylethanol (15): ^{1}H NMR δ 2.86 (s, 6 H), 3.16 (s, 1 H), 3.26 (s, 3 H), 4.95 (s, 1 H), 6.50 (d, 2 H, *J* = 8), 6.86 (d, 2 H, *J* = 8), 7.0–7.4 (m, 8 H), 7.5–7.6 (m, 2 H); ^{13}C NMR δ 40.4, 56.5, 80.7, 86.5, 111.4, 123.6, 126.3, 126.4, 126.7, 127.1, 127.4, 127.8, 129.7, 144.1, 146.2, 149.9. Anal. Calcd for $C_{23}H_{25}NO_2$: C, 79.51; H, 7.25; N, 4.03. Found: C, 79.11; H, 7.36; N, 3.92.

1,1-Diphenyl-2-(indol-3-yl)-2-(4-(*N*,*N*-dimethylamino)-phenyl)ethylene (16): ^{1}H NMR δ 2.81 (s, 6 H), 6.4–7.3 (m, 17 H), 7.6–7.8 (m, 2 H), 8.0 (s, br, 1 H); ^{13}C NMR δ 40.3, 110.7, 111.5, 119.2, 119.6, 121.0, 121.4, 125.5, 126.6, 127.4, 127.5, 127.6, 128.0, 130.8, 131.1, 131.6, 132.0, 134.0, 135.7, 137.6, 144.7, 145.8, 148.8. Anal. Calcd for $C_{30}H_{26}N_2$: C, 86.92; H, 6.32; N, 6.76. Found: C, 86.52; H, 6.32; N, 6.57.

1,1-Dibenzoyl-2-(4-(*N*,*N*-dimethylamino)phenyl)ethane (9): A mixture of 4-(benzotriazol-1-ylmethyl)-*N*,*N*-dimethylaniline (**1b**) (0.63 g, 2.5 mmol), dibenzoylmethane (0.56 g, 2.5 mmol), and anhydrous zinc bromide (0.84 g, 3.75 mmol) in dry toluene was heated under reflux for 27 h, cooled, poured into aqueous NaOH solution (10%, 30 mL), extracted with ether, and dried over $MgSO_4$. The solvent was evaporated to give an oil, which upon flash column chromatography on silica gel using petroleum ether/EtOAc (15:1) as eluate gave the desired product (0.22 g, 25%): ^{1}H NMR δ 2.84 (s, 6 H), 3.37 (d, 2 H, *J* = 6.6), 5.51 (t, 1 H, *J* = 6.6), 6.60 (d, 2 H, *J* = 8.8), 7.11 (d, 2 H, *J* = 8.8), 7.3–7.5 (m, 6 H), 7.89–7.91 (m, 4 H); ^{13}C NMR δ 34.2, 40.6, 59.4, 112.8, 126.8, 128.5, 128.7, 129.5, 133.3, 136.0, 149.3, 195.5.

Aromatic Alkaloids from the Marine Sponge *Chelonaplysilla* sp.

Steven C. Bobzin and D. John Faulkner*

Scripps Institution of Oceanography, University of California, San Diego, La Jolla, California 92093-0212

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Four novel alkaloids derived from tryptophan and tyrosine subunits have been isolated from the marine sponge *Chelonaplysilla* sp. collected from a marine lake in Palau. The structures of chelonin A (**3**), chelonin B (**4**), bromochelonin B (**5**), and chelonin C (**6**) were determined by interpretation of spectral data and chemical conversions. Chelonin A (**3**) and C (**6**) are the first natural products incorporating a 2,6-disubstituted morpholine ring. Chelonin A (**3**), chelonin B (**4**), and bromochelonin B (**5**) exhibited antimicrobial activity against *Bacillus subtilis*, while chelonin A (**3**) showed in vivo antiinflammatory activity.

We have previously reported[1] the isolation of several diterpenes from a sponge of the genus *Dendrilla* collected from a marine lake in Palau. This sponge has now been reclassified as a member of the genus *Chelonaplysilla*.[2] The diterpenes isolated from this *Chelonaplysilla* sp. include 1-bromo-8-ketoambliol A acetate (**1**) and related compounds and rearranged spongian diterpenes exemplified by dendrillolide A (**2**). Chemical studies of the same *Chelonaplysilla* species collected in Pohnpei resulted in

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